This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-63 (canceled)

64. (currently amended) A device for adhering a biomolecule in a predetermined position comprising:

a substrate having thereon a plurality of cytophilic regions that can adhere a biomolecule [on the substrate by] and cytophobic regions to which the biomolecules do not adhere wherein cytophobic regions are contiguous with the cytophilic regions, and

wherein the cytophobic regions comprise one or more surfactant compounds.

65. (previously added) The device of claim 64 wherein the surfactant compound is not covalently linked to the substrate.

66. (previously added) The device of claim 64 wherein the surfactant compound comprises one or more hydrophobic regions and one or more hydrophilic regions.

67. (previously added) The device of claim 64, wherein the surfactant compound comprises one or more heteroatoms.

68. (previously added) The device of claim 64, wherein the surfactant compound comprises one or more alkoxy groups.

69. (previously added) The device of claim 64, wherein the surface of the device comprises a polymeric material.

70. (previously added) The device of claim 64, wherein the surfactant comprises

polyethylene oxide.

71. (previously added) The device of claim 64, wherein the surfactant comprises polyC_{3-20}alkyl oxide.

72. (previously added) The device of claim 64, wherein the surfactant comprises thiol groups.

73. (previously added) The device of claim 64, wherein the cytophilic regions comprise biomolecules adhered thereto.

74. (previously added) The device of claim 64, wherein the cytophilic regions comprise cells adhered thereto.

75. (previously added) The device of claim 74, wherein cytophilic regions comprise two or more different cell types.

76. (previously added) The device of claim 74, wherein the cells are of the same cell type.

77. (previously added) The device of claim 64, wherein the cytophilic regions comprise binding agents for binding the biomolecule.

78. (previously added) The device of claim 64, wherein the device is in the form of a block.

79. (previously added) The device of claim 64, wherein the device comprises a plurality of raised features.

80. (previously added) The device of claim 79, wherein the surface of the device is corrugated.

81. (previously added) The device of claim 64, wherein the device comprises microfluidic channels.

82. (previously added) The device of claim 81, wherein the channels comprise cytophilic and cytophobic regions.

83. (previously added) The device of claim 64, wherein the device is substantially planar.

84. (previously added) The device of claim 64, wherein the cytophilic regions are for adhering cells and the distance between regions permits intercellular contact.

85. (currently amended) The device of claim 64, wherein the cytophilic regions are for adhering cells and are interconnected so as to form a network of contacting cells when cells are adhered thereto.

86. (previously added) The device of claim 64, wherein the regions are aligned to form parallel patterns of alternating cytophilic and cytophobic regions.

87. (previously added) The device of claim 73, wherein the biomolecules comprise nucleic acids.

88. (previously added) The device of claim 73, wherein the biomolecules comprise polypeptides.

89. (currently amended) The device of claim 64, wherein the [device] substrate comprises polydimethylsiloxane.

90. (currently amended) The device of claim 64, wherein the device [comprises] is in the form of a slide, chamber, particles, wire, container, capillary, stamp, tubing, sphere, microtiter plate, nanotube, assay plate, microchip, or implantable device and the substrate comprises a surface of the device.

91. (newly added) The device of claim 64, wherein the substrate is polymeric.

92. (newly added) The device of claim 64, wherien the substrate is hydrophobic.

Pending Claims

Claims 64-90 are pending. Claims 64, 85, 89 and 90 are amended. Claims 91 and 92 are added; thus, upon entry of this amendment claims 64-91 are presented for examination. Support for the amended claims may be found throughout the specification and figures and as further detailed in the paragraph below.

Claims 75-90 Are Rejected Under 35 U.S.C. § 112, First Paragraph

Claims 75-90 are rejected under 35 U.S.C. § 112, first paragraph for containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time that the application was filed had possession of the invention. The Examiner asserts that support for the claims is not readily apparent in the specification.

Applicants respectfully traverse the rejection as support is found throughout the specification for each of the claim limitations of claims 75-90 as shown in the summary table below.

Claim	Support (at least at):
Claim 75:.... wherein cytophilic regions comprise two or more different cell types.	See, e.g., Figures 5D and 5E which show micrographs of devices comprising *hepatocytes and fibroblasts*. See also description of Figure 5D and 5E on page 9. See additionally, page 16, lines 12-3, "The methods of the present invention enable the co-culture *of two or more cell types, e.g., hepatocytes and fibroblasts*." See, also page 16, last paragraph, "the combination of previous methods of photolithographic patterning with fluidic delivery of cels allows both the creation of isolated islands and patterning of *multiple cell types* with a limited number of ligands."
Claim 76: ...wherein the cells are of the same cell type.	See, e.g., Figure 5B which shows *a single cell type* (hepatocytes) and description of Figure 5B on page 9.

Claim	Support (at least at):
Claim 77: ...wherein the cytophilic regions comprise binding agents for binding the biomolecule.	See, e.g., page 7, lines 15-20, "The cytophilic areas are created by the surface itself, or alternatively, by the immobilization of binding agents on the surface." See, also, page 8, lines 5-15, describing that the binding agents /sytophilic regions can be separated from each other by cytophobic regions compirsing a compound that is non-adhesive of the biological molecule or cell. See, also page 10, last paragraph which defines the term "binding agent" and page 17, lines 1-21 which provides numerous examples of binding agents.
Claim 78: ... wherein the device is in the form of a block.	See, e.g., Figure 1A.
Claim 79: ... wherein the device comprises a plurality of raised features.	See, e.g., page 29, lines 20-31, discloses devices generated by photlithographic patterning, "a simple method to produce isolated structures (i.e., islands) with varying periodicity and size and shape." See also page 18, lines 15-16 which discloses that the surface may be corrugated or rugose.
Claim 80 wherein the surface of the device is corrugated.	See, e.g., page 18, lines 15-16, "The surface may be corrugated, rugose, contoured, concave, convex or any combination of these."
Claim 81 wherein the device comprises microfluidic channels.	Page 16, lins 1-2, discloses "direct localization of cells throug injection of cells into microfluidic channels..." See, also, e.g., page 29, lines 18-20, :Fluidic channel networks were molded by casting PDMS on a pre-fabricated template...."
Claim 82: ... wherein the channels comprise cytophilic and cytophobic regions.	See, e.g., page 29, lines 20-24, which discloses that "channels with adhesive or non adhesive chemical species which can spontaneously adsorb or be covalently coupled to the surface facilitated localized immobilization on the underlying, chemically-uniform substrate"
Claim 83:... wherein the device is substantially planar.	See, page 17, lines 29-30, "The substrate may be substantially planar, although it need not be according to certain embodiments."
Claim 84:... wherein the cytophilic regions are for adhering cells and the distance between regions permits intercellular contact.	See, e.g., page 20, lines 5-6, "For instance, if it is desirable to have some cell to cell interaction, the islands may be patterned to be close enough together for intercellular contact."

Claim	Support (at least at):
Claim 85: ... wherein the cytophilic regions are for adhering cells and are interconnected so as to form a network of cells when cells are adhered thereto.	See, e.g., page 20, lines 5,-6, "..if it desirable to have some cell to cell interaction the islands may be patterned to be close enough together for intercellular contact." See, also page 20, lines 10-12, "In one embodiment of the invention the cytophiclic regions are interconnected to form a circuit, e.g., to form a network of cells."
Claim 86:...wherein the regions are aligned to form parallel patterns of alternating cytophilic and cytophobic regions	Page 20, lines 14-15, "In yet another embodiment, the adhesive regions are aligned to form a parallel pattern of adhesive and non-adhesive regions."
Claim 87:... wherein the biomolecules comprise nucleic acids.	Page 6, lines 18-23, "A wide variety of biomolecules may be adhered to a substrate in accordance with the invention and include, e.g., ...nucleic acids....". See also original claim 26.
Claim 88:... wherein the biomolecules comprise polypeptides.	Page 6, lines 18-23, "A wide variety of biomolecules may be adhered to a substrate in accordance with the invention and include, e.g., ...polypeptides...." See also original claim 26.
Claim 89: ... wherein the substrate comprises polydimethylsiloxane.	Page 29, lines 16-18, "In contrast, Figure 4B depicts a patterning scheme for extracellular matrix, PEO, and direct cell localization via a fluidic delivery system constructed from polydimethylsiloxane (PDMS)."
Claim 90: ... wherein the device is in the form of a slide, chamber, particles, wire, container, capillary, stamp, tubing, sphere, microtiter plate, nanotube, assay plate, microchip, or implantable device and the substrate comprises a surface of the device.	Page 17, lines 26-30, "the surface material may comprise any biological, non-biological organic, or inorganic material, or a combination of any of these existing as particles, strands, precipitates, gels, sheets, tubing, spheres, containers, capillaries, pads, slices, films, slides, etc."
Claim 91: ....wherein the substrate comprises a polymeric material.	See, e.g., page 6, lines 24-25 which discloses that substrates include polymeric substrates. See also page 7, lines 12-13, :"the surface of these devices surface [sic] comprises polymeric materials, PLGA, polyimide, polystyrene, glass, metal, and the like." See, additionally, page 18, lines 1-9, particularly line 6, which discloses that an example of a substrate is "polymer coated glass."
Claim 92:...wherein the substrate is hydrophobic.	See, Brief Description of drawings, for example, at description of Figure 6.

Accordingly, in view of the above, Applicants respectfully submit the rejection is improper and should be withdrawn.

Claims 64-90 Are Rejected Under 35 U.S.C. § 112, Second Paragraph

Claims 64-90 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and claim the subject matter which Applicants regard as the invention

The Examiner objects, in particular, to certain terms.

Claim 64: "on the substrate by cytophobic regions"

Applicants respectfully submit that the rejection of this claim is now moot in view of Applicants' amendment above.

Claim 65 is said to be confusing by requiring the surfactant compound to not be covalently linked to the substrate since claim 64 requires the cytophobic regions to contain the surfactant. The Examiner suggests that the term "substrate" in claim 65 be changed to "cytophobic regions."

Applicants traverse the rejection as claim 64 encompasses the scenario wherein surfactant is either covalently or non-covalently linked to the substrate (thereby forming cytophobic regions) and thus the meaning of claim 65 would not be unclear to those of skill in the art. For example surfactant molecules may be covalently linked or chemisorbed. The latter scenario is described at least at page 12, lines 4-11 and at page 15, lines 8-15. Claim 65 thus further limits claim 64 by reciting an aspect of the invention where the surfactant compounds are not covalently linked.

Claim 69 is said to be unclear as to the meaning and scope of "the surface of the device comprises a polymeric material". The Examiner inquires whether this means that the polymeric material is coated on the device or that the device is formed from the polymeric material.

Applicants respectfully traverse the rejection as the claim encompasses either possibility and is not unclear in this regard. See, e.g., page 6, lines 24-25 which discloses that substrates include polymeric substrates. See also page 7, lines 12-13, :"the surface of these devices surface [sic] comprises polymeric materials, PLGA, polyimide, polystyrene, glass, metal, and the like." See, additionally, page 18, lines 1-9, particularly line 6, which discloses that an example of a substrate is "polymer coated glass."

In *claim 78*, the Examiner asserts that meaning and scope of "block" is uncertain.

Applicants respectfully traverse the rejection as the meaning of a "block" is neither relative nor ambiguous and should be accorded its common meaning in the art , i.e., a solid structure with flat sides, for example, as shown in Figure 1A.

Claims 79-81 are said to be unclear "as to the relationship of the structure required to the substrate and cytophilic and cytophobic regions required in claim 64."

Applicants respectfully traverse the rejection. As discussed throughout the specification, the surface of the substrate may have a number of configurations including comprising a plurality of raised features (see, e.g., as discussed in the table provided above). The raised features may comprise cytophilic while non-raised portions of the device may comprise cytophobic regions. The raised features may comprise cytophobic regions while the non-raised portions comprise cytophilic regions. Additionally, or alternatively, some raised features may comprise cytophilic regions while other raised features comprise cytophobic regions. Any of these aspects of the invention is encompassed within the scope of the claim and would be understood to those of skill in the art.

Claim 82 is also said to be unclear "as to the relationship of the cytophilic and cytophobic regions

required to the cytophilic and cytophobic regions required by claim 64." The Examiner inquires if the regions of claim 82 are in addition to those of claim 64.

Applicants respectfully traverse the rejection. Claim 64 recites that the device comprises cytophobic and cytophilic regions that are contiguous to each other. The open language of the claims encompasses additional cytophobic and cytophilic regions that may not be contiguous to one another. Claim 82 recites a device comprising microfluidic channels comprising cytophilic ad cytophobic regions which may or may not be contiguous to one another. Applicants respectfully submit that the langauge of the claims is not ambiguous and would be understood to those of skill in the art.

Claim 85 is said to be unclear as to the meaning of "interconnected so as to form a network of cells". The Examiner states that the meaning and scope of "network of cells" is uncertain and that it would be uncertain as to when cells are a network and not a network.

Applicants respectfully traverse the rejection as applied to amended claim 82. As disclosed in the specification, cells may be patterned onto the device in a pattern which permits intercellular contact, thereby allowing them to form a network of cells which are able to communicate with each other or be interconnected. See, e.g., page 20, lines 5,-6, "..if it desirable to have some cell to cell interaction the islands may be patterned to be close enough together for intercellular contact." See, also page 20, lines 10-12, "In one embodiment of the invention the cytophiclic regions are interconnected to form a circuit, e.g., to form a network of cells." Applicants submit that the language of the amended claim would be clear to those of skill in the art.

Claim 89 is said to be unclear as to the part of the device that contains the polydimethylsiloxane. Does this material form the device or does it have some other function?

Applicants respectfully submit that the rejection is moot in view of the amendment to the claim which recites that the substrate contains polydimethylsiloxane.

Claim 90 is said to be confusing because it is unclear as to how the structures required further modify the structure of claim 64. Also, how do these structures function in relation to the structure of claim 64?

Applicants respectfully submit that the rejection is moot in view of the amendment to the claim which recites that the device is in the form of a slide, chamber, particles, wire, container, capillary, stamp, tubing, sphere, microtiter plate, nanotube, assay plate, microchip, or implantable device and the substrate comprises a surface of the device.

In view of the above amendments and arguments, Applicants respectfully request that the rejections be reconsidered and withdrawn.

Claim 64-90 Are Rejected Under 35 USC § 103(a)

Claims 64-90 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,368,838 B1 by Singhvi, et al. ("Singhvi") in view of WO 96/15223 by Dewez, et al ("Dewez"). The Examiner asserts that Singhvi discloses a device having cytophilic islands for adhering cells and cytophobic regions which isolate the cytophilic islands. The Examiner cites Dewez as disclosing a biomaterial for selective adhesion of cells or tissue, which contains a

polymeric support having a heterogeneous surface conditioned with a surfactant and an extracellular matrix protein. The extracellular matrix protein adheres to one surface area of the support and the surfactant adheres to another surface area where it inhibits adsorption of the extracellular matrix protein (paragraph bridging pages 3 and 4). Cells preferentially adhere to the portion of the support containing the extracellular matrix protein (page 4, lines 12-16).

The Examiner asserts that would have been obvious to provide the cytophilic islands of the device of Singhvi with extracellular matrix protein to enhance the binding of cells as suggested by Singhvi et al and Dewez and it would have been obvious to provide the cytophobic regions of Singhvi with a surfactant to inhibit binding of extracellular matrix protein to these regions as suggested by Dewez. The Examiner makes the unsupported statement that the conditions of dependent claims would have been matters of obvious choice within the skill of the art in view of the disclosures of the references.

Applicants respectfully traverse the rejection. In Singhvi, cytophobic regions are created by SAMS. Singhvi does not disclose or suggest the use of surfactants to create cytophobic regions. While Dewez does disclose the use of surfactants to create cytophobic regions, Dewez employs plasma treatment to modify the surface of the substrate and Dewez provides no reasonable expectation of success that that a surfactant could be used on an untreated surface to provide cytophobic regions. Thus, Dewez also provides no motivation to modify the surfaces of Singhvi to include a cytophobic region which is a surfactant as Dewez would not lead one to expect that surfactants would adhere without a prior plasma treatment step.

Additionally, Singhvi's method simply would not work using a polymeric material as claimed in claims 69 and 91, as SAMS require a metal substrate. Thus, the references in combination do not result in Applicant's invention as recited in these claims. Further, the substrates of Dewez are not hydrophobic as required in newly added claim 92. Plasma treatment changes the surface of a substrate such that whatever is in the plasma (e.g., O_2, N_2) binds to the